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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/623,150	07/18/2003	Anne Marie Heegaard	59573(46865)	5193

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Edwards & Angell, LLP
Intellectual Property Practice Group
P.O. Box 55874
Boston, MA 02205

EXAMINER	
DUNSTON, JENNIFER ANN	
ART UNIT	**PAPER NUMBER**
1636	

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09/19/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/623,150	HEEGAARD ET AL.	
	Examiner	Art Unit	
	Jennifer Dunston	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 March 2007 and 28 June 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *9,11,18,21-23 and 27* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *9,11,18,21-23 and 27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 6/28/2007 has been entered.

Receipt is acknowledged of an amendment, filed 6/28/2007, in which claims 1-8, 10, 12-17, 19-20 and 24-26 were canceled, and claims 9, 11, and 21 were amended. Currently, claims 9, 11, 18, 21-23 and 27 are pending and under consideration.

Any rejection of record in the previous office actions not addressed herein is withdrawn.

Claim Objections

Claim 23 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. The claim directed to measuring the ability of compounds to block one or more chloride channels and is dependent on claim 18, which limits the chloride channel to ClC-7. This objection was made in the Office action mailed 9/11/2006.

Claim 18 is objected to because of the following informalities: the phrase "the ability to block of the compounds to block the chloride channel C1C-7" should be changed to "the ability of the compounds to block the chloride channel C1C-7" to improve the grammar of the claim.

Claims 21, 22, 23 and 27 depend from claim 18 and are objected to for the same reason applied to claim 18. Appropriate correction is required. This is a new objection.

Claims 9, 11, 18, 21-23 and 27 are objected to because of the following informalities: the claims refer to "C1C", whereas the specification uses the term "CIC." It would be remedial to amend claims 9, 18 and 21-23 to refer to "CIC" channels to be consistent with the nomenclature used in the specification. Appropriate correction is required.

Claims 21, 22, 23 and 27 are objected to because of the following informalities: the claims refer to "a method as claimed in claim 18." It would be remedial to amend the claims to recite "The method of claim 18" so that the dependent claim clearly refers to the method of claim 18. Appropriate correction is required.

Priority

If applicant desires to claim the benefit of a prior-filed application under 35 U.S.C. 119(e), a specific reference to the prior-filed application in compliance with 37 CFR 1.78(a) must be included in the first sentence(s) of the specification following the title or in an application data sheet. For benefit claims under 35 U.S.C. 120, 121 or 365(c), the reference must include the relationship (i.e., continuation, divisional, or continuation-in-part) of the applications.

If the instant application is a utility or plant application filed under 35 U.S.C. 111(a) on or after November 29, 2000, the specific reference must be submitted during the pendency of the application and within the later of four months from the actual filing date of the application or sixteen months from the filing date of the prior application. If the application is a utility or plant application which entered the national stage from an international application filed on or after

November 29, 2000, after compliance with 35 U.S.C. 371, the specific reference must be submitted during the pendency of the application and within the later of four months from the date on which the national stage commenced under 35 U.S.C. 371(b) or (f) or sixteen months from the filing date of the prior application. See 37 CFR 1.78(a)(2)(ii) and (a)(5)(ii). This time period is not extendable and a failure to submit the reference required by 35 U.S.C. 119(e) and/or 120, where applicable, within this time period is considered a waiver of any benefit of such prior application(s) under 35 U.S.C. 119(e), 120, 121 and 365(c). A benefit claim filed after the required time period may be accepted if it is accompanied by a grantable petition to accept an unintentionally delayed benefit claim under 35 U.S.C. 119(e), 120, 121 and 365(c). The petition must be accompanied by (1) the reference required by 35 U.S.C. 120 or 119(e) and 37 CFR 1.78(a)(2) or (a)(5) to the prior application (unless previously submitted), (2) a surcharge under 37 CFR 1.17(t), and (3) a statement that the entire delay between the date the claim was due under 37 CFR 1.78(a)(2) or (a)(5) and the date the claim was filed was unintentional. The Director may require additional information where there is a question whether the delay was unintentional. The petition should be addressed to: Mail Stop Petition, Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

If the reference to the prior application was previously submitted within the time period set forth in 37 CFR 1.78(a), but not in the first sentence(s) of the specification or an application data sheet (ADS) as required by 37 CFR 1.78(a) (e.g., if the reference was submitted in an oath or declaration or the application transmittal letter), and the information concerning the benefit claim was recognized by the Office as shown by its inclusion on the first filing receipt, the petition under 37 CFR 1.78(a) and the surcharge under 37 CFR 1.17(t) are not required.

Applicant is still required to submit the reference in compliance with 37 CFR 1.78(a) by filing an amendment to the first sentence(s) of the specification or an ADS. See MPEP § 201.11.

In the instant case, the reference to the prior application was previously submitted as an amendment to the specification on 7/18/2003. However, Applicant subsequently filed a substitute specification (filed 1/26/2004) that does not include the text of the preliminary amendment. It would be remedial to file an amendment to the specification to include the priority data.

Response to Arguments - Claim Objections

With respect to the objection of claim 23, Applicant's arguments filed 6/28/2007 have been fully considered but they are not persuasive. The response asserts that claim 23 has been amended to limit the chloride channel to CIC-7; however, claim 23 has not been amended. The amendment filed 6/28/2007 indicates that claim 23 was previously presented.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 9, 11 and 23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. This rejection was made over claim 23 in the Office action mailed 9/11/2006 and has been rewritten to include claims 9 and 11.

Claim 9 recites the limitation "the selected chloride channels" in line 7. There is insufficient antecedent basis for this limitation in the claim. It would be remedial to delete this phrase from the claim. Further, line 7 recites the limitation "the channel chemical compound," yet the claim only provides antecedent basis for the term "chemical compound." It would be remedial to delete the word "channel" from the phrase "the channel chemical compound."

Claim 11 depends from claim 9 and is thus indefinite for the same reason applied to claim 9.

Claim 23 recites the limitation "one or more chloride channels of the ClC family" in lines 3, 5 and 6. There is insufficient antecedent basis for this limitation in the claim. In particular, the independent claim 18 has been limited to the ability of compounds to block ClC-7 only.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 9, 11, 18, 21-23 and 27 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for screening chemical compounds for activity in blocking the chloride channel CIC-7 for the treatment of an osteoclast related bone disease in a subject, comprising screening compounds in a test cell so as to select compounds having the ability to block the chloride channel CIC-7 of the CIC family, does not reasonably provide enablement for method for screening a chemical compound for activity in preventing an osteoclast related bone disease or for screening a chemical compound for activity in treating, alleviating or preventing osteopetrosis. The specification does not enable any person skilled in

the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. This is a new rejection.

Enablement is considered in view of the Wands factors (MPEP 2164.01(A)). These include: nature of the invention, breadth of the claims, guidance of the specification, the existence of working examples, state of the art, predictability of the art and the amount of experimentation necessary. All of the Wands factors have been considered with regard to the instant claims, with the most relevant factors discussed below.

Nature of the invention: The nature of the invention is complex in that the claims are drawn to screening assays for the identification of compounds that are capable of preventing any osteoclast related bone disease in a subject through inhibition of CIC-7. Further, claim 27 specifically requires the identification of compounds that are capable of treating, alleviating or preventing osteopetrosis through inhibition of CIC-7.

Breadth of the claims: The claims are broad in that they encompass any osteoclast related disorder. The complex nature of the subject matter of this invention is greatly exacerbated by the breadth of the claims. However, claim 27 is also specifically drawn to osteopetrosis as an osteoclast related disorder.

Guidance of the specification and existence of working examples: The specification teaches that CIC-7 is the only CIC family chloride channel that is expressed in human osteoclasts (e.g., Example 4). Further, the specification teaches that the coordinated transport of protons and chloride ions, by osteoclasts, acidifies the bone resorption compartment, resulting in dissolution of the mineral bone components (e.g., page 2, paragraphs 1-2). Thus, the specification teaches generally that screening for compounds that inhibit CIC-7 will reduce the bone resorption

activity of osteoclasts. These compounds may find use in the treatment of bone disorders that result from too much bone resorption or bone turnover, including osteoporosis, osteolytic cancer invasion, and Paget's disease of bone.

The specification does not teach how to use compounds that inhibit CIC-7 to prevent a representative number of diseases encompassed by the broad claims or to prevent diseases such as osteoporosis, osteolytic cancer invasion, and Paget's disease of bone. Further, the specification does not teach how to treat, alleviate or prevent osteopetrosis with a compound that inhibits CIC-7 activity.

Predictability and state of the art: It would be an unpredictable venture to prevent a representative number of osteoclast related bone disorders encompassed by the claims. For example, Guise (Cancer Supplement, Vol. 88, No. 12, pages 2892-2898, June 2000) teaches that osteolytic cancer invasion results from the presence of tumor cells in the bone (e.g., page 2895, Proposed mechanisms for osteolytic bone metastases). The presence of tumor cells in the bone that secrete PTHrP stimulate osteoclastic bone resorption through the production of RANK ligand and TGFβ (e.g., Guise, page 2895, Proposed mechanisms for osteolytic bone metastases, and Figure 1). The art of record does not teach that CIC-7 plays a role in the metastatic invasion of bone tissue. Thus, it would be unpredictable to prevent the metastatic invasion of bone and subsequent bone resorption using a compound that blocks CIC-7. The prevention of other disorders, such as monogenic diseases or complex traits, would be highly unpredictable to prevent. For example, Paget's disease can occur in children as a result of mutations in the TNFRSF11 B gene, which brings about bone deformity at a young age, which has been improved by treatment (Online Mendelian Inheritance in Man, OMIM (TM). Johns Hopkins

University, Baltimore, MD. MIM Number: #239000: 8/28/2006. World Wide Web URL: http://www.ncbi.nlm.nih.gov/omim/). However, there is no evidence of record that indicates that inhibition of a chloride ion channel in an osteoclast can be used to prevent Paget's disease. Several years after the time of filing, the inventors demonstrate in an osteoporosis animal model that complete prevention of osteoporosis is not possible by treating with a chloride channel inhibitor. Schaller et al (Journal of Bone and Mineral Research, Vol. 19, No. 7, pages 1144-1153, 2004, cited in a prior action) demonstrate only partial protection of bone strength and bone mineral density with one tested compound that may inhibit CIC-7 chloride ion channel (e.g., page 1151). The lack of complete prevention demonstrates the unpredictable nature of using any of the identified compounds or known chloride blockers to prevent osteoporosis or any other osteoclast related bone disease.

It would have also been highly unpredictable to use any CIC-7 inhibitor for the treatment, alleviation or prevention of osteopetrosis. Kornack et al (Cell, Vol. 104, pages 205-215, 2001, cited in the IDS submitted on 2/13/2004) teaches that loss-of-function mutations in the CIC-7 chloride channel result in osteopetrosis. Therefore, further reductions of CIC-7 activity would be expected to result in worsening of symptoms rather than amelioration of symptoms.

Amount of experimentation necessary: A large amount of experimentation would be necessary to determine if the chemical compounds found to block CIC-7 activity or chloride conductance in any test cell would provide compounds for the prevention of any osteoclast related bone disorder. The experimentation would be extensive, because preventative compounds may or may not be identified by the claimed assay. Given that osteopetrosis results

from a lack of CIC-7 activity, experimentation to identify compounds to ameliorate the symptoms or prevent the disease would be expected to result in a complete lack of success.

In view of the breadth of the claims and the lack of guidance provided by the specification as well as the unpredictability of the art, the skilled artisan would have required an undue amount of experimentation to make and/or use the claimed invention. Therefore, claims 9, 11, 18, 21-23 and 27 are not considered to be fully enabled by the instant specification.

Response to Amendment – Declaration of Dr. Morten Karsdal

The declaration of Dr. Morten Karsdal under 37 CFR 1.132 filed 3/16/2007 is sufficient to overcome the rejection of claims 18, 21-23 and 27 based upon insufficiency of disclosure under 35 U.S.C. 112, first paragraph.

Response to Arguments - 35 USC § 112 .

The rejection of claim 10 under 35 U.S.C. 112, second paragraph, has been withdrawn in view of Applicant's amendment to the claims in the reply filed 6/28/2007.

With respect to the rejection of claim 23 under 35 U.S.C. 112, second paragraph, Applicant's arguments filed 6/28/2007 have been fully considered but they are not persuasive.

The response asserts that claim 23 has been amended to correct the insufficient antecedent basis. This is not found persuasive, because claim 23 still requires "one or more chloride ion channels" in the amendment filed 6/28/2007.

For these reasons, and the reasons made of record in the previous office actions, the rejection is maintained.

Applicant's arguments, see pages 4-10, filed 6/28/2007, with respect to the rejection of claims 18, 21-23 and 27 under 35 U.S.C. 112, first paragraph, have been fully considered and are persuasive. The previous rejection of claims 18, 21-23 and 27 has been withdrawn.

With respect to the rejection of claims 9, 11, 18, 21-23 and 27 under 35 U.S.C. 112, first paragraph (scope of enablement presented above), Applicant's arguments filed 6/28/2007 have been fully considered but they are not persuasive.

It is noted that Applicant's comments are directed to the identification of compounds that alleviate symptoms of an osteoclast related bone disease in a subject and are not directed to the prevention of a bone disease (e.g., paragraph bridging pages 7-8 of the reply). Further, the response asserts that the reference to osteopetrosis has been deleted from claim 27 (e.g., response at page 7, 2nd full paragraph); however, claim 27 recites "osteopetrosis" in line 2.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 9, 18 and 21-23 are rejected under 35 U.S.C. 102(e) as being anticipated by Maher et al (US Patent No. 6,686,193 B2; see the entire reference). This is a new rejection.

Regarding claims 9, 18 and 23, Maher et al teach a method for screening chemical compounds for activity in blocking CIC-7, a voltage gated chloride channel, comprising the steps

of (i) providing a cell transfected with a nucleic acid encoding the CIC-7 channel and a control cell that is un-transfected, (ii) subjecting the cells to a chemical compound, and (iii) measuring the ability of the compound to block the voltage gated chloride channel (e.g., columns 46-48, (c) d) Assay of voltage-dependent chloride channels; Table 3).

Regarding claim 21, Maher et al teach the further testing to establish the specificity of the candidate modulator by testing cell lines containing related ion channel family members (e.g., paragraph bridging columns 58-59). Maher et al teach that voltage gated chloride channels related to CIC-7 include CIC-1, CIC-2, CIC-4, CIC-5, CIC-Ka, and CIC-Kb (e.g., Table 3).

Regarding claim 22, Maher et al teach the further screening of the compounds so as to select compounds with specificity for the particular channel being studied (e.g., columns 58-59, d) Selectivity of Candidate Modulators)

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer Dunston whose telephone number is 571-272-2916. The examiner can normally be reached on M-F, 9 am to 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached at 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications

may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Jennifer Dunston, Ph.D.
Examiner
Art Unit 1636

/JD/

CELINE QIAN, PH.D.
PRIMARY EXAMINER